DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

MAY 22 1997

Mr: Samuel Maslak
President
Acuson Corporation
1220 Charleston Road
Mountain View, CA 94043

RE: 95P-0140/CP1

Dear Mr. Maslak:

This letter is in response to your citizen petition requesting the Commissioner of Food and Drugs to use his discretionary authority under 21 CFR 14.1(a)(1) to convene a public hearing before the appropriate public advisory committee(s) to develop criteria for use by FDA for determining when a premarket notification submission (510(k)) is appropriate for diagnostic ultrasound devices and when a premarket approval application (PMA) must be submitted. Cit. Pet. at 1. Specifically, you requested that the panel be instructed to consider claims that devices can distinguish between breast masses that are unquestionably benign from those that are malignant or indeterminate. *Id.* According to your petition, the 510(k) process is routinely used to clear devices with a broad range of diagnostic capabilities, including those that impact on biopsy decisions. *Id.* at 3. You allege that requiring PMAs without panel guidance and public input would amount to a change in the long standing classification of diagnostic ultrasound devices without due process. *Id.* at 2. Moreover, you cite numerous public policy arguments against allowing manufacturers to obtain unnecessary premarket approval for diagnostic ultrasound devices. *Id.* at 4. In accordance with 21 CFR 10.30(e)(2)(ii), FDA is denying your petition for the reasons stated below.

Point 1: The Decision of whether a PMA or 510(k) is required is governed by the statute and implementing regulations.

Under the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 321 *et seq.*) as amended by the Medical Device Amendments of 1976 (the amendments) (Pub. L. 94-295) and the Safe Medical Device Act of 1990 (the SMDA) (Pub. L. 101-629), there are two pathways to marketing a device: the 510(k) process and the premarket approval (PMA) process. The question presented by your petition is when does a new claim for a previously 510(k)'d device trigger the legal requirement for a PMA.

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Under the act, a PMA is to be submitted for a class III device required to have an approval under section 515(b) of the act (21 U.S.C. 360e(b)) or for a device classified into class III pursuant to section 513(f) of the act (21 U.S.C. 360e(f)). A 510(k) submission is the means by which the agency determines whether a device is

substantially equivalent to a predicate device for which premarket approval is not required[1]. Finding a device substantially equivalent to a predicate device permits the device to be marketed and results in the device being included in the same regulatory class and subject to the same requirements as the device to which it is substantially equivalent.

Section 513(i) of the act (21 U.S.C. 360c(i)) defines the term "substantial equivalence." Pursuant to section 513(i)(1)(A) of the act (21 U.S.C. 360c(i)(1)(A)), a device with the same intended use and technological characteristics as a predicate device may be found substantially equivalent to the predicate device. A device with the same intended use as a predicate device, but with different technological characteristics, may be found substantially equivalent to the predicate device only if the manufacturer shows that the new device is as safe and effective as a legally marketed device and does not raise different questions of safety and efficacy, when compared to the predicate device. Id. At the very least, under either circumstance, the new device must have the same intended use as the predicate device for the new device to be found substantially equivalent to the predicate.

This is the critical point. If the new device has a different intended use from the predicate device it will be found not substantially equivalent. The legislative history clearly states: "The legislation requires that a device have the same intended use as any device to which it is determined to be substantially equivalent." See H.Rept. 808, 101st Cong., 2d sess. 25 (1990). In accordance with section 513(f)(1) of the act, if FDA determines that the new device is not substantially equivalent to a predicate device, the device is automatically classified into class III by operation of law and is required to have an approved PMA before it may be marketed. The device remains in class III until the Secretary reclassifies it into either class I or class II.

No assistance by an advisory committee is necessary, therefore, to establish the criteria for determining when a PMA is required for a medical device, including a diagnostic ultrasound device, because such criteria are already established in the act and its implementing regulations.

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[1]A device legally marketed prior to May 28, 1976, or a device which has been reclassified from class III to class II or I.

Point II: The claim identified in your petition is a new intended use for diagnostic ultrasound devices; and

Point III: Your public policy arguments against FDA requiring manufacturers to submit PMAs for diagnostic ultrasound devices with new intended uses are inapplicable.

According to your petition, it is not good public health policy for FDA to require PMAs for indications that reasonably fall within 510(k) review. Cit. Pet. at 11. FDA agrees. The device at issue in your citizen petition, however, included a new specific clinical indication for use for which no ultrasound device had been either approved by the PMA process or cleared by the 510(k) process. This new indication for use constituted a "new" intended use for the device. Accordingly, FDA found the device to be not substantially equivalent to any predicate diagnostic ultrasound devices. As a result of such a finding, the device was automatically classified into class III by operation of law and was required to have an approved PMA before it could be legally marketed.

Approximately 1-3% of devices described in 510(k) submissions are determined to be not substantially equivalent (NSE) to a legally marketed device for which premarket approval is not required. Most of these NSE decisions are based on the device having a new intended use. In particular, we have made NSE decisions when the device changed to a system of artificial intelligence(e.g. identifying suspicious areas and magnifying or enhancing specific areas of tissue for the physician), altering the diagnostic effect of the device in comparison to other legally marketed devices. Examples of the types of technology where these decisions have been made are in radiology (mammography) and pathology (automatic Papanicolaou smears readers).

Your petition states that the practical effect of granting a PMA for any currently available diagnostic claim would render other comparable or superior devices useless. Cit. Pet. at 15. This is not true. Manufacturers who have received premarket clearance under the 510(k) process may continue to market their devices for all cleared intended uses set forth in their original 510(k) submissions. Furthermore, institutions may continue to use the ultrasound devices granted premarket clearance under the 510(k) process. FDA's determination that a PMA is required for a device with a new intended use applies only to that new intended use and in no way affects devices previously cleared through the 510(k) process.

While FDA basically agrees with your position, we recognize that improvements in ultrasound technology may eventually result in information from an ultrasound device being relied on as the predominant factor in rendering a definitive diagnosis. As technology improves and manufacturers claim enhanced diagnostic capability for their

devices, the agency believes that data from clinical trials are necessary to substantiate such claims. From a public health perspective, it is reasonable to continue to clear improvements in imaging technology through the 510(k) process so long as the device design and labeling do not significantly alter the ways in which the device is used in clinical decision making.

You contend that requiring PMAs for ultrasound indications for use which were previously cleared through the 510(k) process will adversely impact the Medicare/Medicaid reimbursement of currently marketed ultrasound devices. Cit. Pet. at 4. As explained above, FDA is not requiring PMAs for ultrasound indications for use which were previously cleared through the 510(k) process. Those products all remain legally marketed devices for their cleared indications, and we know of no basis on which a different coverage decision would be made for those cleared indications for use.

POINT IV: THE AGENCY HAS NOT CHANGED ITS POLICY REGARDING DIAGNOSTIC ULTRASOUND DEVICES.

FDA recently approved the PMA for Advanced Technology Laboratories (ATLs) Ultramark 9 High Definition Imaging Ultrasound System with L10-5 Scanhead. Initially, ATL attempted to submit a 510(k) for the device. However, FDA determined that the manufacturer was required to submit a PMA for the device in order to establish the safety and effectiveness of the device for the new intended use. See Point II.

The ATL PMA application addressed a new indication for use for which no ultrasound device has been either approved by the PMA process or cleared by the 510(k) process. Specifically, the indication is stated in the PMA as follows:

> The device is indicated, as an adjunct to mammography and physical breast examination, to provide a high degree of physician confidence in differentiating benign from malignant or suspicious breast lesions. This device provides the physician with additional information to guide a biopsy decision. Utility of this system has been demonstrated for lesions with an indeterminate level of suspicion (LOS 2-4) by conventional diagnostic modalities. Using this device in the evaluation of solid mass characteristics can reduce the number of biopsies performed on indeterminate lesions.

Although ultrasound devices that have been cleared through the 510(k) process have had intended uses that included a broad range of diagnostic capabilities, none of them

included differentiating solid mass lesions of the breast. FDA determined that this new indication for use constituted a "new" intended use for the device. Thus, in accordance with section 513(i)(1)(A) of the act, FDA determined that the device was not substantially equivalent to any other predicate diagnostic ultrasound device. As a result of such a finding, pursuant to section 513(f)(1) of the act, the device was automatically classified into class III by operation of law and was required to have an approved PMA before it be legally marketed.

In conclusion, the agency has determined that the requested public hearing before a public advisory committee is not necessary because the criteria for determining when to submit a 510(k) or PMA for a diagnostic ultrasound device are well established.

Sincerely yours,

D. Bruce Burlington, M.D.
Director
Center for Devices and
Radiological Health